Factors associated with sarcopenia: a cross-sectional analysis using UK Biobank

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Abstract

Introduction – The critical sociodemographic, lifestyle and diseases factors influencing sarcopenia, defined by the current European Working Group on Sarcopenia 2 (EWGSOP2) classification and cut-off points, have not yet been fully elucidated. This study aimed, therefore, to determine socio-demographic, anthropometric, lifestyle and health-related factors associated with sarcopenia using the new EWGSOP2 definition.

Study design – 396,283 participants (52.8% women, age 38-73 years) were included in this cross-sectional study. The potential factors associated with sarcopenia were allocated to four categories: sociodemographic (sex, age, education, income and professional qualification), anthropometric (nutritional status, abdominal obesity, body fat and birth weight), lifestyle (physical activity, smoking, sleeping and sitting time, TV viewing, alcohol, and dietary intakes) and health status (self-reported prevalent diseases). P-values were corrected for multiple testing using the Bonferroni method.

Results – Age, women, lower education, higher deprivation, underweight, lower birth weight, and chronic diseases such as rheumatoid arthritis, chronic bronchitis and osteoporosis were associated with a higher likelihood of sarcopenia. Conversely, overweight, obese, as well as a self-reported higher intake of energy, protein, vitamins (B12 and B9) and minerals (potassium, calcium and magnesium) were associated with lower odds of sarcopenia.

Conclusion – Women, adults older than 65 years, underweight people and those with rheumatoid arthritis were most likely to have sarcopenia. Considering the increase in the ageing population, sarcopenia is likely to become more prevalent. Identifying factors associated with sarcopenia could inform future strategies for early identification of individuals at high risk of sarcopenia and therefore, the implementation of preventive strategies against the disease.

Keywords: Sarcopenia; Lifestyle; EWGSOP2; Risk factors.

1. Introduction

Sarcopenia is a progressive syndrome characterised by a decline in both the quality and quantity of muscle mass and is associated with a higher risk of disability and lower quality of life [1, 2]. Sarcopenia is an independent risk factor for falls, hospitalisation length, osteoporosis, cardiovascular diseases and mortality [1]. As a result, many interventions have been developed to investigate and attempt to prevent or delay sarcopenia and its associated consequences.

Although previous cross-sectional studies have identified an increasing number of factors associated with sarcopenia; including sociodemographic (age, sex, education) and lifestyle (physical activity and diet) factors [1-7], previous findings have been inconsistent and limited to traditional factors [2, 4, 5]. In this context, extending current evidence to other factors, such as prevalent diseases and micronutrient intake, could help to elucidate novel factors which are associated with sarcopenia and therefore where new interventions could be developed or targeted.

In addition, the European Working Group On Sarcopenia (EWGSOP) has recently updated the sarcopenia definition (EWGSOP2) [1], which has considerably reduced the number of people classified as having sarcopenia because the new definition has decreased the cut-off points of the physical capability markers [8-10]. Therefore, the results from studies that applied the previous definition of sarcopenia may no longer apply. In this context, this study aimed to determine socio-demographic, anthropometric, lifestyle and health-related factors associated with sarcopenia among UK Biobank participants, using the new EWGSOP2 definition.

2. Methods

This was a cross-sectional study, using data collected at the UK Biobank baseline clinic, to assess the associations between different factors and sarcopenia. Due to ethnic differences in the reference values for sarcopenia, inclusion in the study was restricted to white European participants. Further information about UK biobank is available in supplementary methods.

This paper is reported in adherence to the strengthening the reporting of observational studies in epidemiology (STROBE) statement [11].

2.1 Sarcopenia definition

Sarcopenia was defined as low grip strength plus low muscle mass using the current EWGSOP2 classification and cut-off points [1]. More details about sarcopenia classification and its cut-off points are available in supplementary methods.

2.2 Potential factors for sarcopenia

Four categories of factors were investigated: sociodemographic (sex, age, education, income and professional qualification), anthropometric (nutritional status, abdominal obesity, body fat and birth weight), lifestyle (physical activity, sitting time, smoking, sleeping time, TV viewing, alcohol, and macro and micronutrients) and health status (prevalent diseases).

2.2.1 Sociodemographic

Age was calculated from dates of birth and baseline assessment. Townsend deprivation index, professional qualification and gross income were used as measures of area and individual socioeconomic status. Townsend deprivation index was obtained from the postcode of residence and has been derived from four census variables [12]; unemployment, non-car ownership, non-house ownership and household overcrowding. Professional qualifications were self-reported and coded as an ordinal variable; participants were asked, “Which of the following qualifications do you have? A categorical income variable was generated from self-reported income data. Further information in supplementary methods.

2.2.1 Anthropometric

Height was measured to the nearest centimetre (cm) using a Seca 202 height measure, and a Tanita BC-418 body composition analyser was used to measure weight to the nearest 0.1 kg. Both were used to estimate the body mass index (BMI) and the WHO criteria were applied to categorise participants into the following nutritional status: underweight <18.5, normal weight 18.5-24.9, overweight 25.0-29.9 and obese ≥30.0 $kg.m^{-2}$ [13]. Waist circumference (WC) was used to derive abdominal obesity,

defined as ≥88 cm for women or ≥102 cm for men [13]. Body composition was measured using bioimpedance (BIA) by trained nurses. High body fat was defined as body fat ≥ 26.9% in men, and ≥ 38.6% in women. These cut-off points represent the two highest sex-specific quintiles in the UK Biobank population. Self-recalled birth weight was collected at baseline using a touchscreen questionnaire and categorised into tertiles: lower (<3.19 kg), middle (3.19 to 3.63 kg), and higher (>3.63 kg).

2.2.3 Lifestyle

Physical activity was based on self-report using the International Physical Activity Questionnaire (IPAQ) short form [14]. Total physical activity was computed as the sum of walking, moderate and vigorous activity, measured as metabolic equivalents (MET-hours/week). Total time spent in sedentary behaviours was derived from the sum of self-reported time spent sitting and classified as < 4 h/day and ≥ 4 h/day. Watching television was self-reported and categorised as lower (< 2 h/day), middle (3 h/day) and higher (≥ 4 h/day). Self-reported smoking status was categorised as never, former or current smoker and self-reported sleep (<7 h/day, 7 to 9 h/day, and >9 h/day).

Dietary information was collected via the Oxford WebQ; a web-based 24 h recall questionnaire which was developed specifically for use in large population studies and has been validated against an interviewer-administered 24 h recall questionnaire. The Oxford WebQ derives energy intake (total and from specific macronutrients), micronutrients (Vitamins: D, B12, B9 and B6; Minerals: potassium, calcium, magnesium and iron) and alcohol from the information recorded in McCance and Widdowson's The Composition of Food, 5th edition [15]. All these variables were categorised in tertiles: lower, middle and higher intake.

2.2.4 Health status

Medical history at baseline was ascertained from a self-reported physician diagnosis of 345 diseases encoded using the ICD-10. Those diseases with a prevalence ≥1 % in UK Biobank were included in this

study (allergic-rhinitis,, angina, anxiety, asthma, back problem, breast cancer, cataract, chronic bronchitis, depression, dermatitis, diabetes, diverticulitis, gastric reflux, glaucoma, heart attack, hiatus hernia, high cholesterol, hypertension, hypothyroidism, irritable bowel syndrome, migraine, osteoarthritis, osteoporosis, pneumonia, psoriasis, rheumatoid arthritis, stroke, and venous thrombosis). Participants without medical diagnose for any of these 345 diseases were classified as healthy participants and used as the reference group.

2.3 Statistical analyses

Statistical analyses were performed using STATA 15 (StataCorp; College Station, TX). Descriptive characteristics of people with sarcopenia are presented as means with standard deviations (SD) for quantitative variables and percentages for categorical variables. To determine the main sociodemographic, health, anthropometric and lifestyle factors associated with sarcopenia; we used binary logistic regression analysis, where sarcopenia was the outcome coded as 0=normal according to the EWGSOP2 and 1=sarcopenia according to the EWGSOP2. The exposures were fitted into the model as categorical variables. For continuous variables, we derived tertiles of the exposure.

Results are presented as odds ratios (OR) with their respective 95% CI. All analyses were adjusted for confounding factors, including age, sex, deprivation and educational attainment when these were not the exposures of interest. The analyses of smoking and health status were also adjusted for WC.
The p-value used to infer statistical significance was corrected for multiple testing using the Bonferroni method, taking into account the number of comparisons made (n = 56) and the mean correlation between the variables tested. Accordingly, statistical significance was set at $p<0.0008$ for all analyses.

3. Results

Of the 469,858 white participants with information available for the three physical capability markers used to define sarcopenia and severe sarcopenia, 396,283 fulfilled the EWGSOP2 criteria for

sarcopenia and people without sarcopenia and were, therefore, included in the analyses. The main exclusion criteria are presented in Supplementary Figure 1.

The main characteristics of the participants according to their sarcopenia status are presented in Table 1. In summary, 0.4% of the study population had sarcopenia according to EWGSOP2 [1]. Compared to people without sarcopenia, people with sarcopenia were older (mean age 63.0 vs 56.1 years), had a lower height, weight and WC. As a consequence, they had a lower prevalence of overweight, obesity and abdominal obesity, but a higher prevalence of underweight. Furthermore, people with sarcopenia had lower levels of physical activity and reported more falls and fractures in comparison to people without sarcopenia.

The associations of sociodemographic factors with sarcopenia are shown in Figure 1. Women, age older than 56-years-old and lower levels of education were associated with sarcopenia. Underweight participants were almost eight times more likely to have sarcopenia, in comparison to normal-weight individuals (OR: 7.60 [95% CI: 6.08 to 9.50]). Conversely, people who were overweight, obese, or had higher central obesity and body fat were less likely to have sarcopenia (Figure 2). Furthermore, whose birth weight was in the lowest tertile were more likely to have sarcopenia compared to people in the middle tertile (OR: 1.47 [95% CI: 1.26 to 1.72]).

Figures 2 and 3 show the lifestyle factors associated with sarcopenia. Using the corrected p-value, long sleep, watching television more than 4 h/day, being physically active and being a previous smoker, were not significantly associated with sarcopenia in this study. On the other hand, people in the highest tertile of energy and protein intake were less likely to have sarcopenia in comparison to those in the lowest tertile (Figure 3). In terms of micronutrients, a higher intake of vitamins and minerals was associated with a lower odds of sarcopenia. Of these, the highest tertiles of intake for B12, B9, calcium, potassium, and magnesium were all associated with the lowest likelihood of sarcopenia (Figure 3).

Of the 28 diseases analysed, 24 were associated with sarcopenia. The strongest associations were observed for rheumatoid arthritis (OR: 16.3 [95% CI: 12.8 to 20.8]), followed by chronic bronchitis (4.84 [95% CI: 3.49 to 6.70]) osteoporosis (OR: 4.40 [95% CI: 3.56 to 5.46]), stroke (OR: 3.49 [95% CI: 2.33 to 5.22]) and psoriasis (OR: 3.44 [95% CI: 2.25 to 5.26]) (Figure 4).

4. Discussion

The study has shown that using the current EWGSOP2 definition [1], a variety of different sociodemographic (age, women, lower education and higher deprivation), anthropometric (underweight and lower birth weight), and diseases were identified with a higher odds of having sarcopenia. Amongst these risk factors, women, adults older than 65 years, underweight people and those with a diagnosis of rheumatoid arthritis were quantitatively the most likely to have sarcopenia. On the other hand, overweight, obese, as well as those reporting a higher intake of energy, protein, vitamins (B12, B9) and minerals (potassium, calcium, and magnesium), were quantitatively the least likely to have sarcopenia. In this context, this study adds novel evidence to our knowledge of sarcopenia. Taking into account that low levels of physical capability and sarcopenia are strong predictors of premature mortality, cardiovascular and neurodegenerative diseases in the middle- and older-aged populations [16], the current data identifies potentially modifiable factors fundamental for both the prevention and management of the disease. There is also evidence of the potential association between a few novel lifestyle factors (such as longer sleep duration and shorter TV viewing) and sarcopenia risk. However, these factors did not reach the usual threshold of statistical significance after correcting for multiple testing. Further studies will be required to delineate the roles of these factors.

Previous cross-sectional studies have also investigated factors which are more likely to be associated with sarcopenia using different sarcopenia classifications and cut-off points [3, 4, 7]. However, to our knowledge, only one study, on a Japanese population, has used the new definition of sarcopenia to investigate potential risk factors [8]. In that cross-sectional study, Su et al. explored a limited number

of factors associated with sarcopenia and demonstrated that people who had diabetes and those who were taking more than four medications a day were 3.6 and 2.6 times more likely to having sarcopenia [8].

Age, lower levels of education and income have also previously been associated with a higher likelihood of sarcopenia in both European and non-European populations, following the sarcopenia definitions from different working groups [3-6, 17]. In fact, not having a formal education was associated with almost three times higher odds of sarcopenia in a Nigerian population while in Italy, higher education was associated with 15% lower odds of sarcopenia [5, 6]. In contrast, and although women experiment an earlier loss of muscle mass and a major decline in hormones that are important for the muscle (e.g. estrogen), not all studies have identified the same association with sex. Indeed, Santos et al. and Bae & Kim demonstrated that both Brazilian and Korean men were four and three times more likely, respectively, of having sarcopenia than women [3, 18] while Adebusoye et al. showed that Nigerian women had three times higher odds of sarcopenia than men [6]. These differences may be explained by the different diagnostic criteria and cut-off points used to define sarcopenia, and also because of the age of the populations investigated.

During ageing, the risk of malnutrition may occur independently of sarcopenia and other diseases. However, changes in body composition could be another important factor associated with a higher likelihood of sarcopenia[19]. In sarcopenic people, underweight has been associated with a higher likelihood of sarcopenia [7], more often in hospitalised people [20] and even when other cut-off points were used to define underweight (BMI <22kg/m^2)[4]. Although anorexia and underweight are recognised causes of sarcopenia [1], previous studies have highlighted that sarcopenia increases the risk of obesity and poor metabolic health [21]. In other words, obesity exacerbates sarcopenia and vice versa (sarcopenic obesity) [1]. However, and similar to the findings of Han et al. [17] and Volpato et al. [5], in this study, people with higher body weight were less likely to have sarcopenia. A possible explanation may be that obesity represents a possible protective factor against the loss of lean mass in older adults.

Interestingly, and similar to other studies, lower birth weight was positively associated with sarcopenia [2, 22], highlighting the relevance of the correct nutrition and balance even since the intrauterine stage.

Perhaps surprisingly, we did not find any associations between sarcopenia and lower levels of physical activity, sedentary behaviours, smoking, and short and long sleep duration using the corrected p-value. However, other studies have shown a significant association between these factors and sarcopenia. For example, Gianoudis et al. identified that per 1-hour increase in sedentary behaviour the odds of sarcopenia was 33% higher [23] while Steffl et al. demonstrated, in a meta-analysis of 40,007 individuals, that any form of physical activity was associated with a 55% lower likelihood of sarcopenia [24]. Furthermore, Hu et al. showed that sleep duration had a U-shape relationship with sarcopenia, with a higher odds associated with both short (<6 h/day) and long (>8 h/day) sleep durations [25].

In terms of dietary patterns, in the current study, people with a higher intake of energy and protein were less likely to have sarcopenia. However, Granic and colleagues reported different results in the 85+ study (another UK prospective study), since the risk of sarcopenia was higher in people with a traditional British diet, i.e., high in butter, red meat and potato, even when the protein consumption was ≥ 1 g/kg BW/day [26]. Conversely, several vitamins and minerals are important cofactors and essential contributors to muscle, bone, and neurological integrity [27]. As a result, it is no surprise that in this study, higher intake of these nutrients was associated with a lower likelihood of sarcopenia. In fact, higher levels of dietary calcium and vitamin D have been found to be associated with a lower prevalence of sarcopenia [27]. Magnesium, selenium and calcium have also shown to be promising minerals to prevent or treat sarcopenia [28]. However, according to the findings of Beaudart et al., sarcopenic individuals seem to intake lower amount of potassium, magnesium, iron, calcium and vitamins (E and C) in comparison to people without sarcopenia [29].

Two types have been recognised for sarcopenia: primary (associated with age) and secondary (associated with diseases). In this context, chronic obstructive pulmonary diseases, cancer, heart

failure, and diabetes have all been associated with higher odds of sarcopenia [2]. In relation to diabetes, there is evidence of a bi-directional association with sarcopenia [17]. However, using the new EWGSOP2, we did not find any significant association between diabetes and sarcopenia.

According to the EWGSOP2 definition, neurological disorders may become a predisposing factor for sarcopenia as well [1]. In this study, in common with previous studies [30], there was a significant association between sarcopenia and migraine, depression, and anxiety. Finally, it is important to highlight that some acute and chronic illnesses require periods of bed rest or hospitalisation during which muscle quantity and quality may be lost, thereby, contributing to secondary sarcopenia in both middle-aged and old-aged populations [2].

4.1 Limitations

UK Biobank is not representative of the UK population in terms of lifestyle and disease prevalence [31]. Therefore, whilst estimates of effect sizes can be generalised, summary statistics should not. Use of UK Biobank provided the opportunity to test our research question in a very large general population cohort as well as the opportunity to work with information collected using validated and standardised methods. On the other hand, dual-energy X-ray absorptiometry (DXA) is the most commonly used method for deriving muscle mass because it can provide a reproducible estimation of the appendicular skeletal muscle mass in a few minutes. In the UK Biobank, only 5,000 participants had data available for DXA. However, in this study, muscle mass measured using BIA showed a high correlation with DXA ($r=0.868$, $p<0.0001$).

As in any observational study, residual confounding is possible, and due to the cross-sectional study design, temporal relationships could not be established in order to exclude the possibility of reverse causation. Both limitations mitigate against inferring causation. Finally, whilst we were able to study a wide range of factors of interest we could not study all. For example, we did not have data on omega-3 and other antioxidants shown in other studies to be associated with sarcopenia [32]. Therefore, future studies using the EGWSOP2 classification should investigate these factors.

4.2 Conclusions

Multiple sociodemographic, health, anthropometric and lifestyle factors were associated with a higher and lower likelihood of sarcopenia. Among these, women, adults older than 65 years, people with underweight and those with rheumatoid arthritis showed the highest likelihood while being overweight or obese, and a higher intake of energy, protein, vitamins (B12, B9) and minerals (potassium, calcium, and magnesium) showed the lowest likelihood. Considering that with the increase in the ageing population, the illnesses associated are likely to rise as well, public health strategies to prevent or delay ageing diseases are more urgent than ever.

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Authorship Statement

F.P-R, F.K.H, J.P.P and C.C-M contributed to the conception and design of the study, advised on all statistical aspects, and interpreted the data. F.P-R performed the literature search. F.P-R performed the analyses with support from F.K.H, J. P.P and C.C-M. All authors critically reviewed this and previous drafts. All authors approved the final draft for submission. F.K.H, J.P.P and C.C-M contributed equally to this work and are joint senior authors. C.C.-M. is the guarantor.

Data statement

All UK Biobank information is available online on the webpage www.ukbiobank. Data access are available through applications. This research was conducted using the application number 7155.

Conflict of interest

None to declare.

Words:

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Table 1. Characteristics population without and with sarcopenia

	No sarcopenia (normal)	Sarcopenia
Socio-demographics		
Total n	394,605	1,678
Prevalence (%)	(83.9%)	(0.4%)
Age (years), mean (SD)	56.1 (8.1)	63.0 (5.3)
Deprivation index, mean (SD)	-1.6 (2.9)	-1.3 (3.0)
Smoking status, n (%)		
Never	215,924 (54.9)	993 (59.5)
Previous	138,609 (35.2)	529 (31.7)
Current	38,877 (9.9)	147 (8.8)
Obesity-related markers		
Height (meters), mean (SD)	1.69 (0.09)	1.61 (0.07)
Body weight (kg), mean (SD)	78.0 (15.2)	59.6 (8.3)
BMI, mean (SD)	27.1 (4.4)	22.9 (2.9)
BMI Categories, n (%)		
Underweight (<18.5 $kg.m^{-2}$)	1,480 (0.4)	102 (6.1)
Normal weight (18.5-24.9 $kg.m^{-2}$)	131,731 (33.5)	1,171 (69.8)
Overweight (25.0 to 29.9 $kg.m^{-2}$)	173,553 (44.1)	392 (23.3)
Obese (≥30.0 $kg.m^{-2}$)	86,692 (22.0)	13 (0.8)
Waist Circumference (cm)	89.7 (12.9)	78.2 (8.8)
Central Obesity, n (%)	121,990 (31.0)	224 (13.4)
% Body fat, mean (SD)	30.7 (8.3)	36.1 (6.4)
Fitness and Physical activity		
Total PA ($MET.h^{-1}.week^{-1}$), mean (SD)	3018.3 (3286.7)	2609.6 (2744.5)
TV viewing ($h.day^{-1}$), mean (SD)	2.7 (1.5)	3.2 (1.7)
Total Sedentary behaviour ($h.day^{-1}$), mean (SD)	5.0 (2.2)	4.6 (2.0)
Health status, n (%)		
Diabetes history	15,062 (3.8)	28 (1.7)
CVDs history	106,513 (27.0)	443 (26.5)
High blood pressure history	88,983 (22.6)	343 (20.5)

Fractures	19,919 (56.5)	201 (80.1)
Falls, n (%)		
No falls	326,585 (82.9)	1,189 (70.9)
Only one fall	49,217 (12.5)	354 (21.2)
More than one fall	18,218 (4.6)	133 (7.9)

BMI: body mass index; n: number; $h.day^{-1}$: hour/day; PA: physical activity; MET: metabolic-equivalent;; SD: standard deviation; CVD: cardiovascular disease;

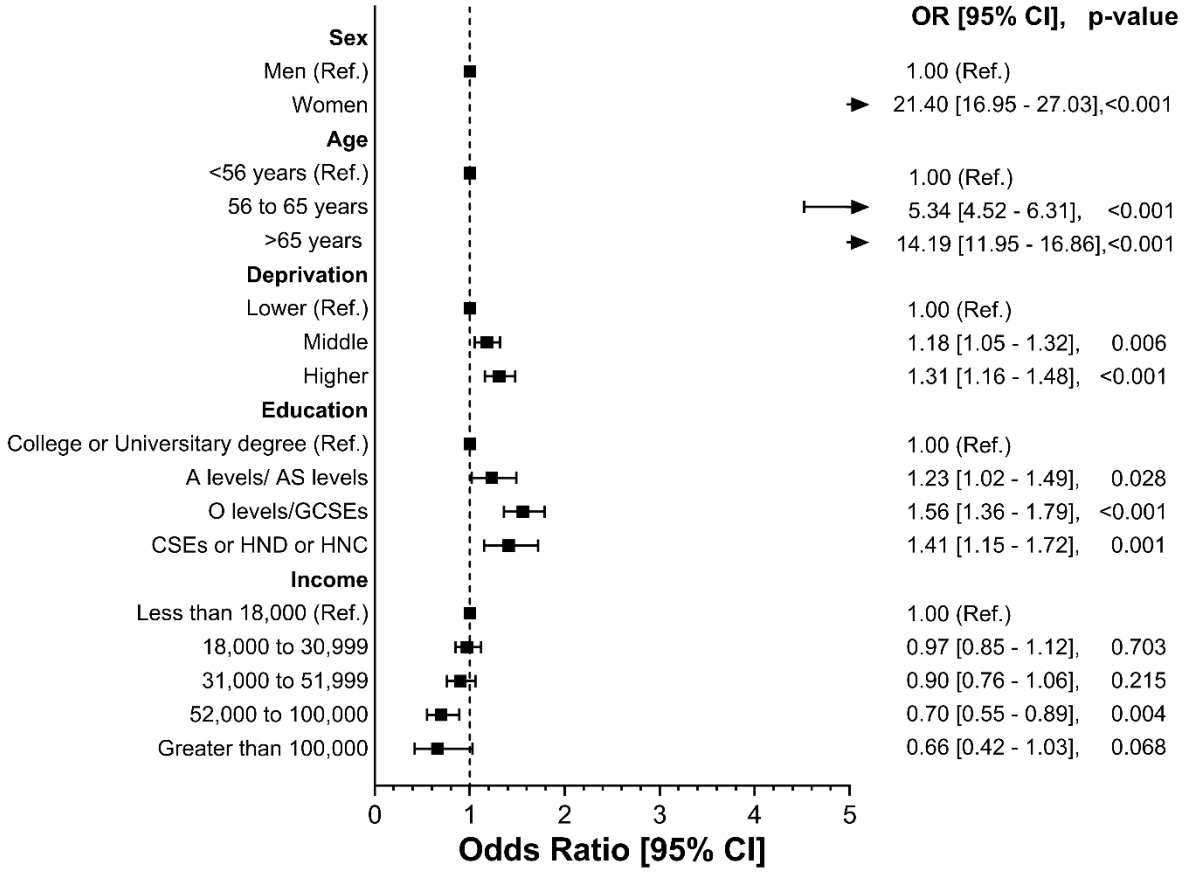

Figure 1. Sociodemographic factors associated with sarcopenia.

Data are presented as odds ratios (OR) with their respective 95% CI. All analyses were adjusted for confounding factors, including age, sex, deprivation and education attainment when these were not the exposure.

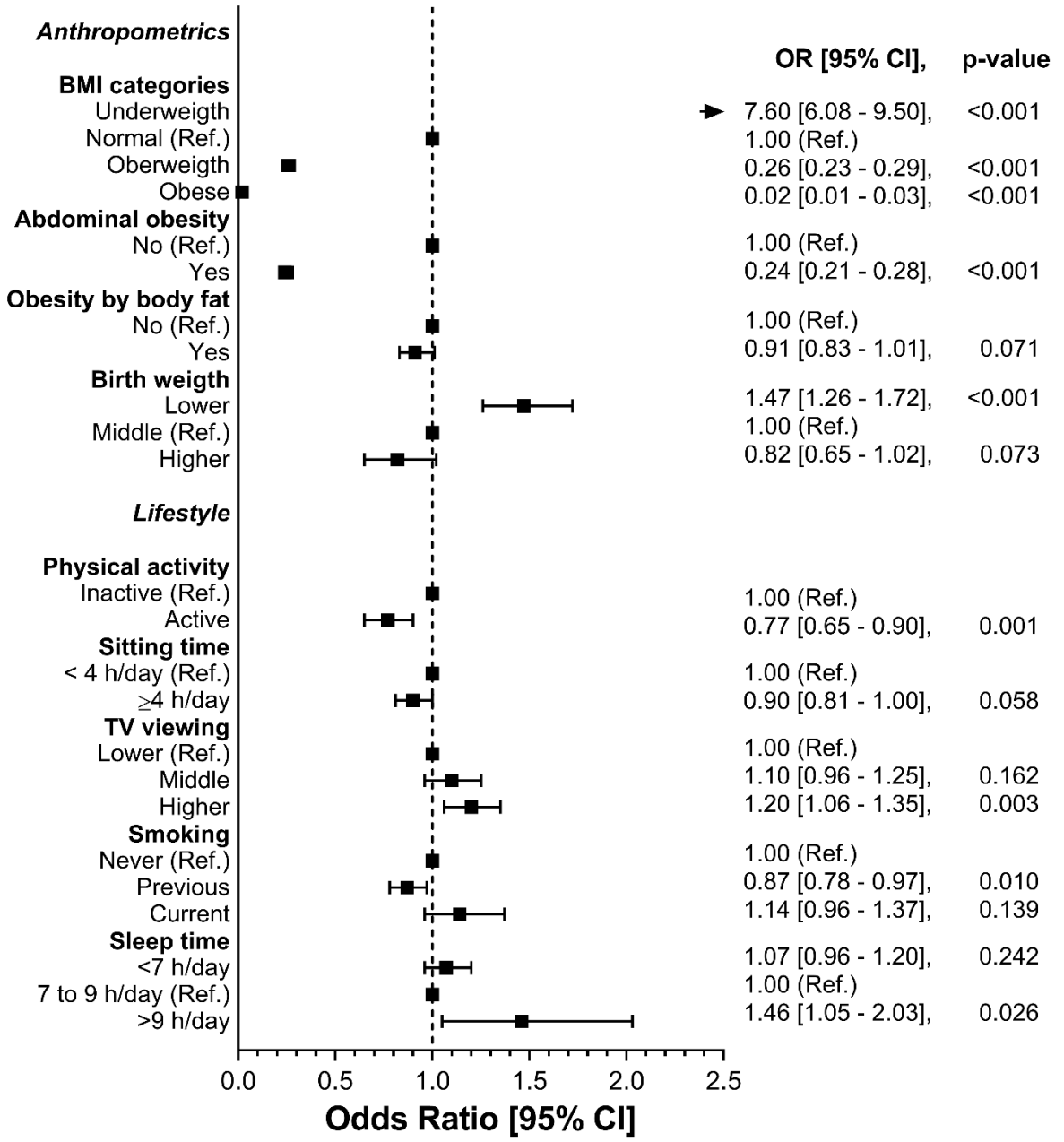

Figure 2. Anthropometric and Lifestyle factors associated with sarcopenia..

Data are presented as odds ratios (OR) with their respective 95% CI. All analyses were adjusted for confounding factors, including age, sex, deprivation and education attainment. Besides, smoking was further adjusted by WC.

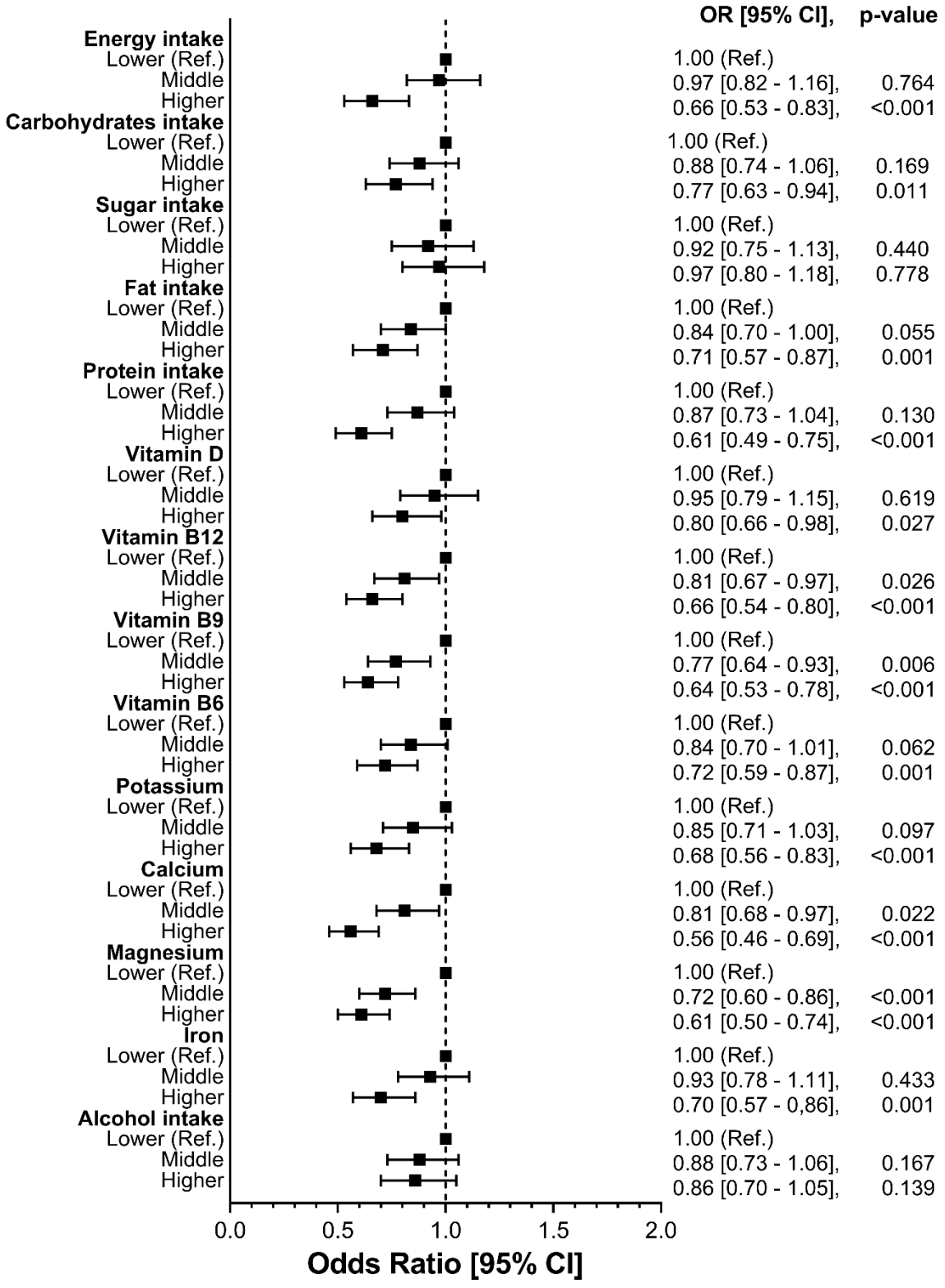

Figure 3. Nutritional factors associated with Sarcopenia.

Data are presented as odds ratios (OR) with their respective 95% CI. All analyses were adjusted for confounding factors, including age, sex, deprivation and education attainment.

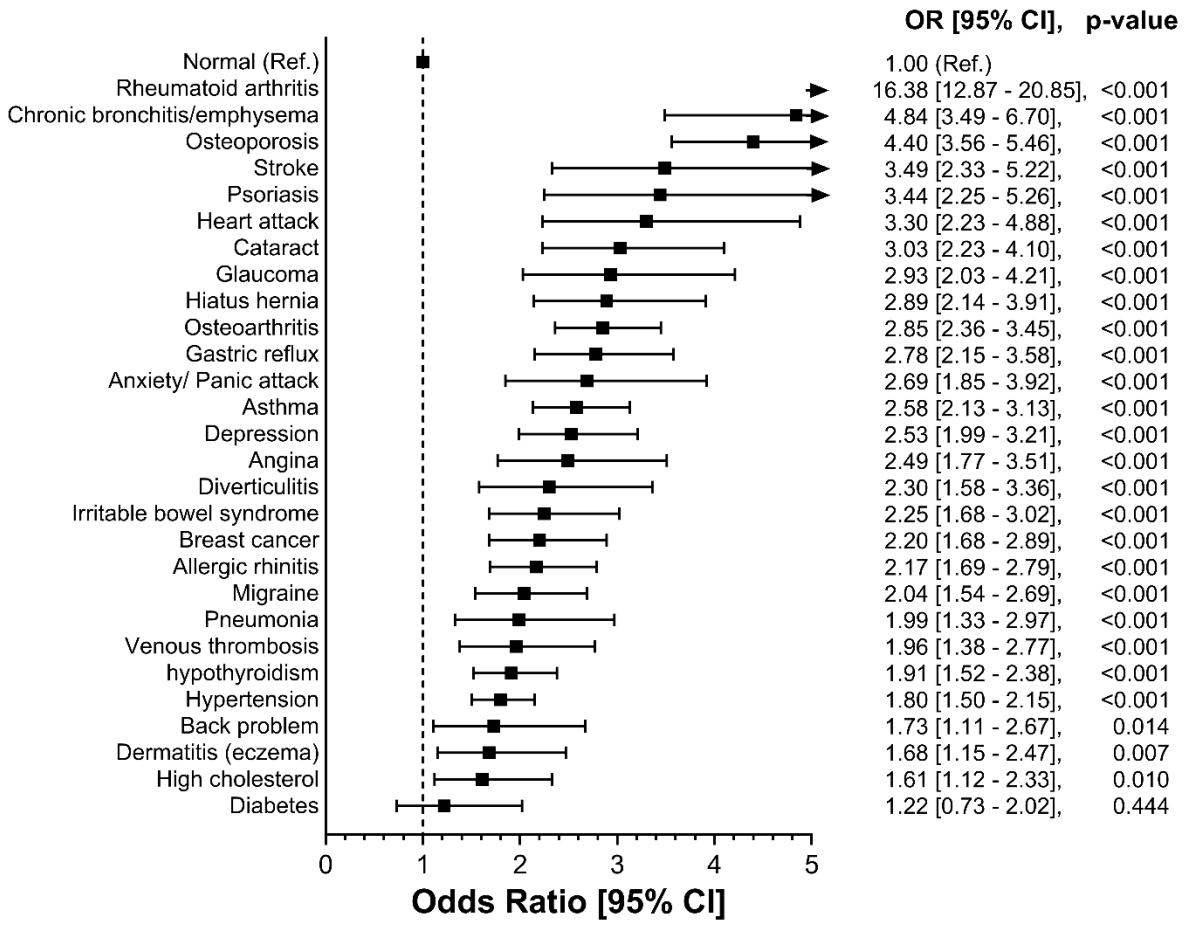

Figure 4. Diseases associated with sarcopenia.

Data are presented as odds ratios (OR) with their respective 95% CI. All analyses were adjusted for confounding factors, including age, sex, deprivation and education attainment and WC.